



# Effect of testosterone therapy on breast density in transmasculine individuals: A pilot study.

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# Clinical Relevance Statement

- Characterizing breast tissue density in transmasculine people will clarify the effect of testosterone therapy on breast tissue density, improve understanding of their breast cancer risk factors, and support the development of screening guidelines for this vulnerable community.



# Background

- Transmasculine individuals (assigned female at birth) may pursue testosterone therapy (TT) to enhance masculinization *and affirm their gender identity*.
- The effect of long-term exposure of the biologically female body to TT is unclear.
- TT modulates breast histology<sup>1</sup>, however, it is unknown whether TT alters breast tissue density, and in turn, the breast cancer risk of transmasculine individuals.

1. Baker GM, et al. 2021. Modern Pathol. 34, 85–94.



# AIM

- To investigate the relationship between the duration of TT and breast tissue density in transmasculine individuals, using both qualitative and quantitative metrics.



# Materials and Methods

- We established a retrospective cohort of 444 transmasculine individuals who underwent chest-contouring surgery at our institution (2013-2019)<sup>1</sup>.
- Patient clinical data were retrieved from the medical records.
- Among these 444 subjects, 42 had mammograms taken between 0.4 to 34.9 months prior to surgery and qualitative tissue density assessments.

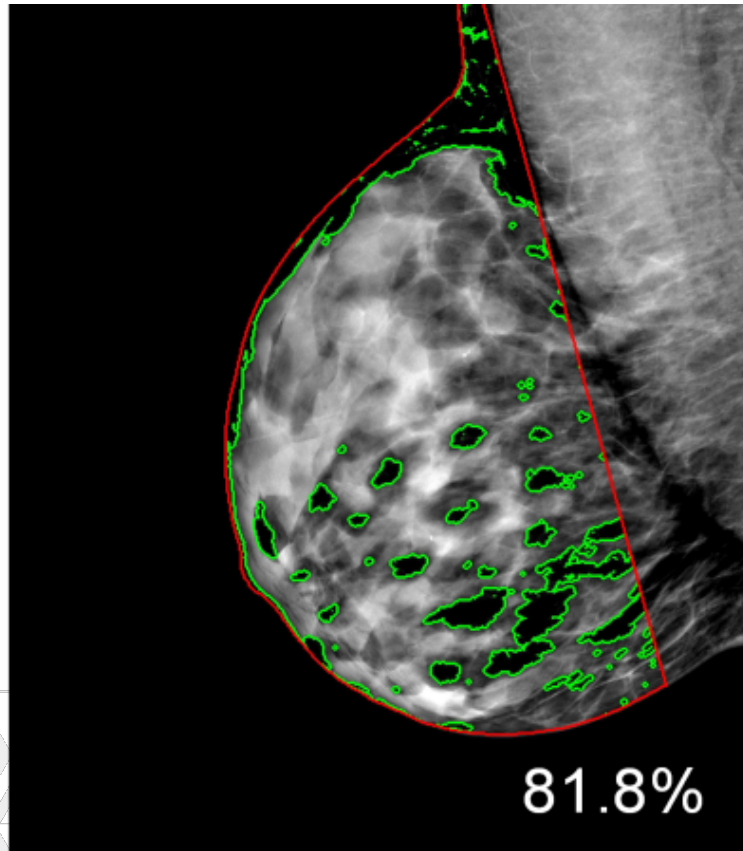
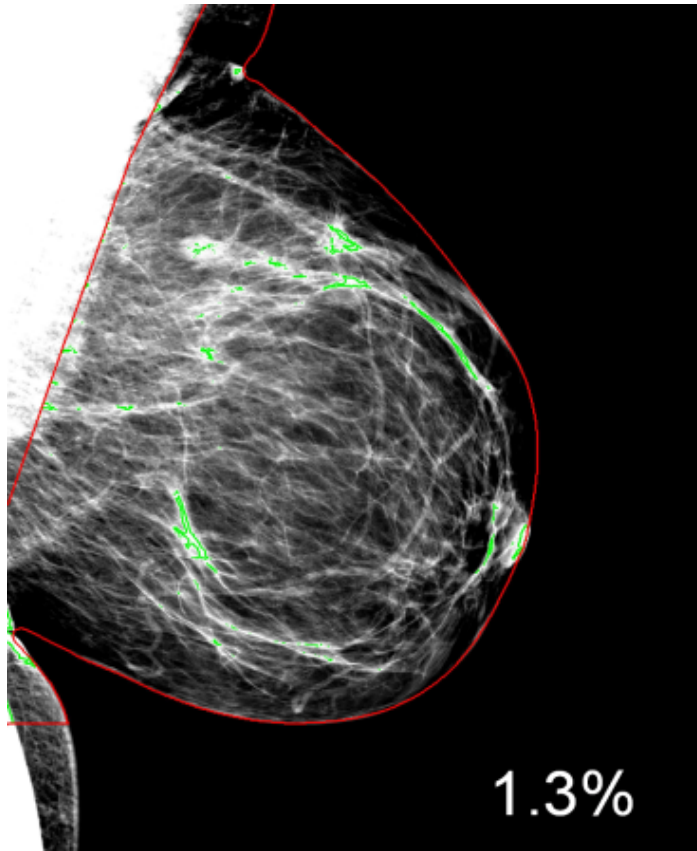
1. Baker GM, et al. 2019. Transgender Health. 4, 326–330.

# Materials and Methods (continued)

- Mammogram images (DICOM files; 2 to 3 mediolateral oblique views) were available for 25/42 individuals.
- DICOM files were processed using the LIBRA software to extract % breast density <sup>1</sup>.
- Average % breast density was calculated and square root transformed for analysis.

1. Keller BM, et al. Medical Physics. 39, 4903–4917.

**Figure 1.** LIBRA extracted percentage mammographic densities from DICOM files; examples from 2 transmasculine individuals.



# Results

- Among the 42 individuals (median age of 43; range=20-61) with pre-operative mammograms:
  - 6 (14.3%) had fatty breasts,
  - 13 (31.0%) had scattered fibroglandular densities,
  - 18 (42.9%) had heterogeneously dense breasts, and
  - 5 (11.9%) had extremely dense breasts (Table 1).



**Table 1.** Characteristics of 42 transmasculine individuals who had mammograms prior to chest contouring surgery.

	Total (n=42)	DICOM files available (n=25)	DICOM files missing (n=17)	p-value
Age at surgery, median [IQR]*	43.3 [37.8, 48.5]	38.8 [30.6, 45.5]	46.1 [39.5, 49.3]	0.084
Ethnicity, n (%)				0.333
White	33 (78.6)	18 (72.0)	15 ( 88.2)	
Black or African-American	6 (14.3)	5 (20.0)	1 ( 5.9)	
Asian	1 ( 2.4)	0 ( 0.0)	1 ( 5.9)	
Mixed race	1 ( 2.4)	1 ( 4.0)	0 ( 0.0)	
Native American/Pacific Islander	1 ( 2.4)	1 ( 4.0)	0 ( 0.0)	
BMI* at surgery, median [IQR]	28.5 [24.6, 30.0]	28.7 [25.7, 30.1]	26.5 [24.1, 29.8]	0.497
Chest binding				1.00
Yes	19 (45.2)	16 (94.1)	3 (100.0)	
No	1 ( 2.4)	1 ( 5.9)	0 ( 0.0)	
Unknown	22 (52.4)	-	-	



**Table 1.** Continued.

	Total (n=42)	DICOM files available (n=25)	DICOM files missing (n=17)	p-value
Length of testosterone use				0.125
<1 year	12 (28.6)	8 (32.0)	4 ( 23.5)	
>=1 to <2 years	7 (16.7)	6 (24.0)	1 ( 5.9)	
>=2 to <5 years	9 (21.4)	6 (24.0)	3 ( 17.6)	
Never use	14 (33.3)	5 (20.0)	9 ( 52.9)	
Breast density, assessed by radiologists				0.494
Fatty (A)	6 (14.3)	3 (12.0)	3 ( 17.6)	
Scattered fibroglandular (B)	13 (31.0)	7 (28.0)	6 ( 35.3)	
Heterogenously dense (C)	18 (42.9)	13 (52.0)	5 ( 29.4)	
Dense (D)	5 (11.9)	2 ( 8.0)	3 ( 17.6)	



# Results (continued)

- No association between TT (yes/no) and breast tissue density among all individuals ( $p=0.63$ ), or within individuals  $<40$  years old ( $p=0.91$ ) or  $\geq 40$  years old ( $p=0.88$ ; Table 2).

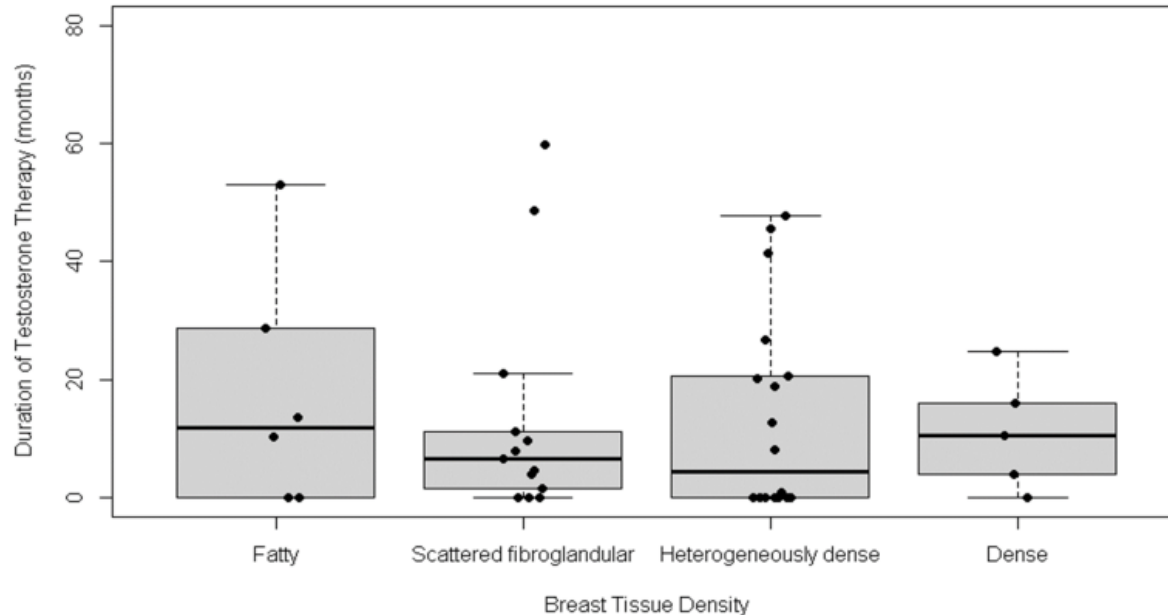
**Table 2.** Breast density (by radiologists) stratified by age ( $<40$  and  $>40$  years old) and TT.

	<40 years old		>40 years old	
	TT (yes)	TT (no)	TT (yes)	TT (no)
<i>n</i>	14	6	14	8
Breast density, assessed by radiologist				
Fatty (A)	3 (21.4)	1 (16.7)	1 (7.1)	1 (12.5)
Scattered fibroglandular (B)	4 (28.6)	1 (16.7)	6 (42.9)	2 (25.0)
Heterogenously dense (C)	4 (28.6)	3 (50.0)	6 (42.9)	5 (62.5)
Dense (D)	3 (21.4)	1 (16.7)	1 (7.1)	0 (0.0)



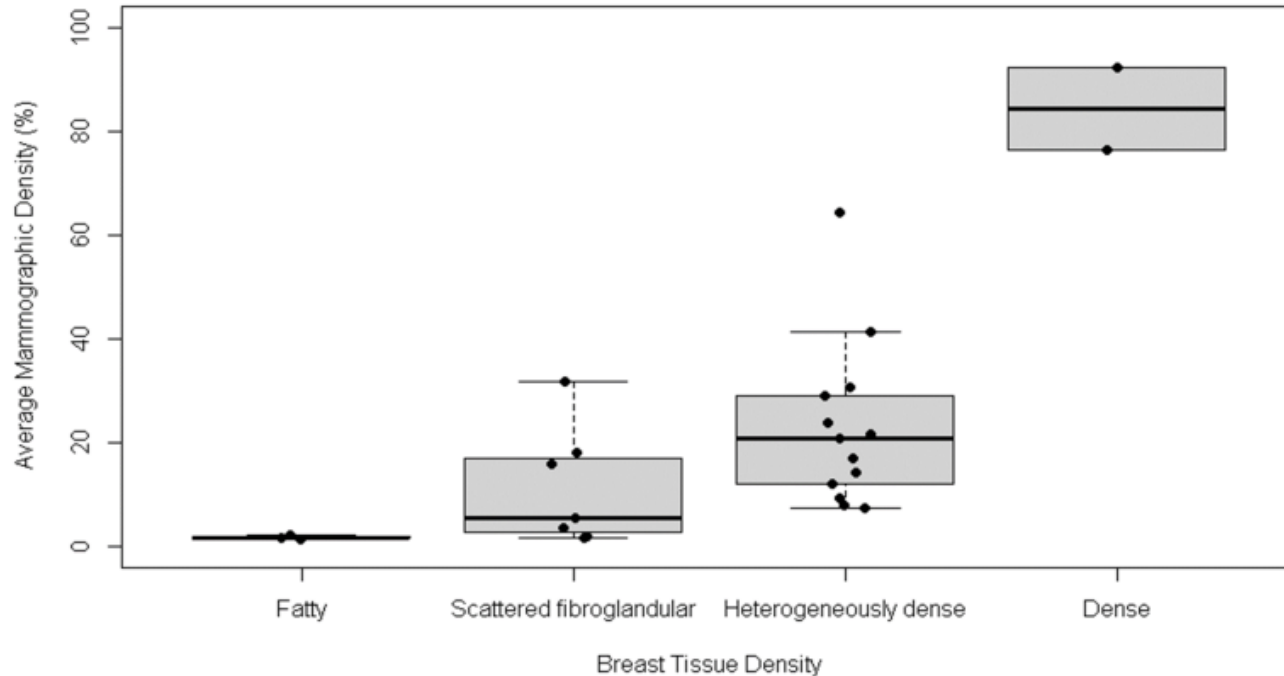
- No association between duration of TT (median=8.0 months; range=0-59.7) and breast tissue density ( $p=0.93$ ; Figure 2).

**Figure 2.** There was no association between duration of TT and breast density assessed by radiologists ( $p=0.93$ , Kruskal-Wallis test).



- Breast density assessed by radiologists was significantly correlated with calculated average % breast density ( $\rho = 0.67$ ;  $p < 0.001$ ; Figure 3).

**Figure 3.** Breast density assessed by radiologists was significantly correlated with average % breast density computed using LIBRA ( $\rho = 0.67$ ;  $p < 0.001$ ).



# Results (continued)

- No association between TT (yes/no) and % breast density ( $\beta=-1.52$ ,  $p=0.20$ ) or when the linear regression model accounted for age at mammogram and BMI at surgery ( $\beta=-0.39$ ,  $p=0.69$ ).
- Similar null associations were also observed between duration of TT and % breast density (crude  $\beta=-0.04$ ,  $p=0.14$ ; adjusted  $\beta=-0.01$ ,  $p=0.52$ ).

# Conclusion

- In this pilot study, gender-affirming testosterone therapy does not appear to affect the breast tissue density of transmasculine individuals.
- Larger studies are needed to confirm these findings.



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Thank you!

